Investigators Study Effects of Remifentanil Given Prior to Cesarean Section. Ngan Kee et al. (page 14)

Anesthesiologists have reported cases of remifentanil used during induction of general anesthesia for cesarean section in women with preeclampsia and other conditions, to modulate maternal heart rate and blood pressure. However, no controlled studies to date have monitored effects on neonates at birth after use of remifentanil for induction purposes. Ngan Kee et al. devised a randomized, double-blind, controlled study to investigate the matter.

Enrolling 40 women with singleton pregnancies scheduled for elective cesarean section, the team randomly allowed the participants to receive an intravenous bolus of either 1 µg/kg remifentanil or saline immediately before induction of general anesthesia. Patients received ranitidine or famotidine orally the night before their scheduled procedures. Using standard monitoring, the team assessed blood pressure, heart rate, and mean arterial pressure throughout the study period. After delivery, neonates were assessed by a pediatrician blinded as to maternal group assignment. Time to sustained respiration, any resuscitative measures required, and Apgar scores at 1 and 5 min after birth were all recorded.

The women receiving remifentanil registered a smaller increase in systolic arterial pressure after induction than did those receiving saline solution. The Apgar scores and time to sustained respiration were similar between the two groups of neonates. However, two neonates delivered from mothers in the remifentanil group were considered clinically depressed and were given naloxone. The single bolus of remifentanil effectively attenuated hemodynamic changes after induction of anesthesia and tracheal intubation in the mothers. However, because the drug crosses the placenta and produced side effects in the neonates, the researchers advise that the drug should be used for clear maternal indications only when adequate facilities for neonatal resuscitation are available.

Duration of Block with Lidocaine–Prilocaine Mixture Tested in Rats. Söderberg et al. (page 110)

Investigators continue to search for the ideal vehicle for accomplishing long-term nerve blocks for the treatment of chronic pain. In this issue, Söderberg et al. report on their efforts to develop a physically stable and easily injectable depot preparation of local anesthetics in which the concentration could be varied between 0 and 100%. The team prepared six lipid formulations, containing 2.0, 5.0, 20, 40, 60, or 80% of lidocaine:prilocaine (1:1, by weight) in medium-chain triglyceride. All formulations were oily liquids at room temperature and could be injected through a 29-gauge needle. Saline solutions of lidocaine:prilocaine HCl were prepared at 0.40 and 2.0% strength, and a sterile 99.5% ethanol solution was used as an active control in one experiment.

In three separate randomized experiments, the team assessed the duration of sciatic nerve block and local neurotoxicity after administration of 10 different preparations. Based on the outcome of nerve block experiments, two formulations (the 20% and 60% lidocaine:prilocaine in medium-chain triglyceride) underwent further studies. Rats receiving the 20% formulation demonstrated a threefold duration of sensory block compared to those receiving the 2% aqueous solution, while rats receiving the 60% formulation experienced blocks 180 times those of the aqueous solution group. In the higher concentration formulations (80% and 100%) all animals still showed nerve block 2 weeks later. However, lidocaine:prilocaine formulations of 60% or greater produced significant neurotoxic effects, as did the ethanol solution. In vivo investigations of time for 50% release revealed a clear difference between the aqueous solution and lipid formulations. The in vivo release of local anesthetic, the team found, could be approximately predicted from in vitro data for the lower formulation (20%) but not the 60% formulation. Although the possibility of using a high-concentration local anesthetic depot formulation for long-term nerve blocks exists, the authors caution that further investigation is needed before these could replace the standard use of ethanol or phenol.

Susceptibility to Ventilator-associated Lung Injury after Endotoxin Exposure. Schreiber et al. (page 133)

Schreiber et al. designed a study to investigate the relationship between transient systemic inflammation and lung injury after mechanical ventilation. They exposed one group of rats to a transient endotoxin challenge by injecting them with a nonlethal dose of Escherichia coli endotoxin. After 24 h, both control (phosphate buffered saline)treated and endotoxin-treated rats were randomized to undergo either no mechanical ventilation or mechanical ventilation with varying tidal vol-
umes (tidal volumes of 8, 24, 27, or 30 ml/kg body weight). There were 10 rats in each treatment group.

Animals who received endotoxin but were not in a ventilation group showed no symptoms of clinical illness 24 h later, although their lung neutrophil counts were increased. For rats undergoing mechanical ventilation, body temperature was maintained at 38°C, and heart rate, arterial and central venous blood pressures, peak airway pressure, and arterial blood gases were recorded every 30 min. After 4 h of mechanical ventilation, the animals were killed and their lungs harvested for histologic examination.

Compared to the animals in control groups, those receiving high tidal volume ventilation showed stronger pulmonary inflammatory responses and more severe lung injury. This injury was demonstrated by impaired oxygenation, increased lung wet-to-dry weight ratios, and increased levels of protein, neutrophils, and cytokines in lung lavage fluid. Animals treated with endotoxin who later received low tidal volume ventilation had an inflammatory response but did not show pulmonary impairment. The 24-h delay after systemic injection of endotoxin, in this animal model, resulted in an increased susceptibility to the deleterious effects of increasing tidal volume. Avoiding high tidal volume in patients who have recovered from a period of endotoxemia might be advisable.

Deciphering the Analgesic Action of Preoperative Cyclooxygenase-2 Inhibitors. Fornai et al. (page 152)

Fornai et al. designed a double-blind randomized trial to assess whether prostaglandin production at the surgical site accounts for the analgesia associated with use of cyclooxygenase-2 (COX-2) blockade in the preoperative period. They administered 50 mg rofecoxib (a selective COX-2 inhibitor), 550 mg naproxen (a nonselective COX-1/COX-2 inhibitor), or placebo preoperatively to patients who were scheduled to undergo removal of an impacted third molar.

The team collected gingival specimens during tooth removal and 240 min after surgery. They also evaluated patients’ subjective pain using categorical and visual analogue scales every 30 min beginning an hour and a half after surgery. Cyclooxygenase-1 and COX-2 mRNA expression was examined by reverse-transcription polymerase chain reaction in the gingival specimens collected.

The team found that pain intensity and prostaglandin E$_2$ production in the placebo group increased throughout the observation period. Preoperative naproxen prevented pain and decreased prostaglandin production at all time points. Rofecoxib produced pain relief throughout the entire observation period, and reduced prostaglandin production from 150 min onward, compared to placebo. At the end of the observation period, COX-1 mRNA expression was unchanged, whereas COX-2 mRNA was significantly induced. Although preoperative administration of a selective COX-2 inhibitor confers effective control of postoperative oral surgical pain, the selective blockade of inducible COX-2 at the peripheral level does not entirely explain the analgesic action of the drug in the postoperative period.

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